TABLE 2.—Smoking characteristics of silica-exposed workers

Study	Number and type of population		Smoking characteristics (percent)			Comments
Prowse (1970)	240 gold miners, South Africa		SM 57	EX* 30	NS 12	* Not smoked in last 6 months
Brinkman et al. (1972)	301 automotive industry workers, aged 40–65		SM 65.8	NS/EX 34.2		
		Light (1–200)*	11			* Numerical rating of cigs/day × years smoked
		Moderate (201–600)	22.3			
		Heavy (≥600)	32.5			
Sluis-Cremer (1972)	Men exposed to dust, Carletonville, South Africa	Exposed workers	70	30		
		Nonexposed workers	60.7	39.3		
Theriault et al. (3 papers) (1974)	792 granite workers, Vermont		SM 60.4	EX 25.6	NS 13.9	
Armstrong et al. (1979)	Coal and gold miners, Australia		SM	NS/EX		
		Gold miners	66.3	33.7		
Rom et al. (1983)	Trona miners, Wyoming		42.8	33.6	23.6	

NOTE: SM = Smoker; EX = Ex-smoker; NS = Nonsmoker.

Epidemiological Findings

Early observers of occupational diseases, including Ramazzini in 1713 (1964), wrote about the respiratory problems of miners and stone cutters, and recognized silicosis among miners, stone cutters or hewers, and potters. Silicosis, and its previously described associated health effects, have been given a variety of names that reflect the several faces of silica exposure—dust consumption, ganister disease, grinders' asthma, grinders' consumption, grinders' rot, grit consumption, masons' disease, miners' asthma, miners' phthisis, potters' rot, rock tuberculosis, stonehewers' phthisis, and stonemasons' disease (Hunter 1955). Greenhow (1878), in his treatise on bronchitis, recognized that "irritants which act immediately upon the bronchial membrane may produce inflammation by means of either mechanical or chemical irritation. Fine coal and metal dust, stone and porcelain grit, and even the flue of cotton wool . . . inhaled into the lungs during various industrial processes are all of them mechanical irritants which become fruitful causes of bronchitis in certain classes of operatives" (p. 30).

Mortality studies of silica-exposed cohorts have consistently shown increased mortality rates for tuberculosis and nonmalignant respiratory disease, largely accounted for by silicosis (Guralnick 1962; Registrar General 1958, 1978; Davis et al. 1983; Armstrong et al. 1979; McDonald et al. 1978; Fox et al. 1981). Although none of these studies accounted for the effects of smoking, the consistency and magnitude of the increased rates suggest a causal relationship between silica exposure and these cause-specific mortality rates. Davis and colleagues (1983) demonstrated dose–response relationships between exposure category, tuberculosis, and silicosis, but found no excess mortality from bronchitis and pneumonia. Finkelstein and colleagues (1982) investigated mortality among 1,190 Ontario miners receiving compensation awards for silicosis and found nonmalignant respiratory disease (excluding tuberculosis) to be the most frequent cause of death (standard mortality rate, 765).

NIOSH recently assessed causes of disability among employees of the mining industry, based on the Social Security Disability Benefit Awards and Allowances to Workers for 1969–1973 and 1975–1976 (Osborne and Fischbach 1985). The observed proportional morbidity rate (PMR) for pneumoconiosis from silica and silicates (they were not distinguished) was found to be somewhat higher (4,894) than for other mining occupations. Workers employed in boring, drilling, and cutting jobs appeared to experience increased disability from respiratory diseases, specifically pneumoconiosis including silicosis. These findings, based on somewhat more recent exposures than the previously cited mortality studies, confirm the major mortality findings, but suffer from the same methodological problems. Again, smoking data were not available or analyzed, and it is recognized

that those disabled in the mid-1970s very likely were exposed to silica three or four decades previously; therefore, their disabilities reflected previous dust exposures.

Early morbidity studies of workers exposed to silica dust focused on rates of sickness, respiratory symptoms, and physical findings, supplemented in the 1920s with chest radiography. The U.S. Public Health Service (US PHS) conducted the first major U.S. silicosis study of the hard-rock mining industry in 1913–1915 (Higgins et al. 1917; Lanza and Higgins 1915). Their studies reported that 60.4 percent of the 720 miners examined suffered from pulmonary diseases attributable to mine rock-dust exposure. Dust samples collected with a Draeger liter bag–granulated sugar filter apparatus were reported to average from 30 to 50 mg/m^3 (Higgins et al. 1917). Although these concentrations would appear to be quite high, they are difficult to interpret according to modern-day respirable dust sampling and analysis (x-ray diffraction for free silica content).

Subsequent US PHS silica studies included Harrington and Lanza's (1921) 1916–1919 study of copper miners in Butte, Montana, in which 42.4 percent were judged to have some dust-induced lung injury and 25.5 percent to have advanced disease. Dreessen and colleagues (1942) studied 727 metal miners in 1939, and Flinn and colleagues (1963) studied 67 underground mines employing 20,500 miners from 1958 to 1961, but found varying silicosis prevalence from mine to mine and widely divergent exposures to free silica. The silicosis prevalences of 9.1 percent and 3.4 percent, respectively, were found to be associated with longer duration of exposure and especially with face work exposures (Dreessen et al. 1942; Flinn et al. 1963). Earlier, Flinn and colleagues (1939) had reported an important study (1936–1937) of West Virginia potteries that included 2,516 workers with an overall silicosis prevalence of 7.8 percent. Free silica content ranged from 1 to 39 percent, dust concentrations varied from 3 to 440 million particles per cubic foot (mppcf), and mean particle diameters were judged to be 1.2 μm (but without data on the concentration of respirable dust). A strong dose–response relationship between dust concentration, duration of pottery exposure, and silicosis prevalence was documented. It was suggested that no new cases of silicosis would occur if dust concentrations in this industry were brought below 4 mppcf. Renes and colleagues (1950) studied 18 ferrous foundries in 1948–1949, and found 9.2 percent of 1,937 foundrymen to have pulmonary fibrosis. Free silica content averaged 30 percent, with a mean particle size of 3 μm, and 82 percent of the samples had levels below 6.9 mppcf. Mechanical shakeout operations were found to have the highest dust concentrations (10 to 75 mppcf), and silicosis was noted to be more prevalent among foundrymen with 20 or more years of exposure. It was suggested that conditions had improved in foundries and that most of the pulmonary fibrosis was

due to previous exposures. Early studies of the refractory (silica) brick industry documented high percentages of free silica, often in the form of cristobalite and tridymite from burned bricks. Keatinge and Potter (1949) and Fulton and colleagues (1941) studied 1,035 exposed workers in this industry, finding 52 percent to have some stage of silicosis. A relationship with dust concentration and duration of exposure was again documented, as was an apparent increased risk among men exposed to burned brick dust (Keatinge and Potter 1949; Fulton et al. 1941).

Epidemiological studies of workers in the Vermont granite industry have provided an important and interesting chronology of data on the natural history of silica-associated respiratory diseases. Early US PHS studies of this industry (Russell et al. 1929) documented high dust concentrations (37 to 59 mppcf) and a very high prevalence of silicosis. On the basis of dust with a free silica content of 35 percent, a presumptive "safe limit" of dustiness was suggested to lie between 9 and 20 mppcf. A subsequent US PHS study (Russell 1941) essentially confirmed the findings of the original study, noted an increased progression of silicosis among the highly exposed cutters, and concluded that a limit below 10 mppcf for this industry would be desirable. Subsequent followup studies in 1955 by the US PHS and the Vermont State Board of Health (Hosey et al. 1957) found that the prevalence of silicosis had decreased from 45 percent in 1937–1938 to 15 percent in 1956, that the silica content of the dust averaged a somewhat lower 22 to 25 percent free silica, and that nearly all workers with silicosis had been exposed prior to implementation of dust controls in 1937. This report was consistent with an earlier report by Ashe (1955), and was subsequently supported by a further followup study by Ashe and Bergstrom (1965), which reported no cases of silicosis among 1,478 granite workers employed after 1937, and a study by Davis and colleagues (1983) that reported only one case in the same population.

All of these early studies of silica exposure concentrated on radiographic evidence of silicosis and tuberculosis and the association with silica content and concentration. These studies formed the basis for environmental control of silica exposures, demonstrated the effectiveness of dust control, and provided a widely held impression that silica exposures, and hence disease arising from silica exposures, were well controlled.

Beginning in the 1950s, British epidemiologists introduced standardized respiratory questionnaires, field spirometry, and sound epidemiological methodology to the study of bronchitis and chronic obstructive lung disease, and were the first to use these methods to assess respiratory effects among industrial workers. This allowed assessment of other risk factors, including cigarette smoking, and quantitation of major risk factors compared with appropriate

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reference populations. At the same time, on the basis of clinical case series, it was becoming clear that bronchitis and nonspecific airways obstruction were more common than pneumoconiosis among workers exposed to coal mine dust and silica dust. The significance of these health effects was not clear. Modern epidemiological studies began with the Higgins and colleagues (1959) investigation of Stavely, an English industrial town of 18,000 and home to a significant number of coal miners and foundry workers. This study and other cross-sectional studies of silica exposure that have assessed standardized respiratory symptoms, lung function, smoking, and occupation (only those with non-coal-mining silica exposures) are summarized in Table 3.

Review of these studies has found them to be heterogeneous in regard to workforce composition, free silica content and dust concentration (if reported), and other associated occupational exposures that may contribute to respiratory symptoms and declines in lung function. In some instances associated occupational exposures other than silica dust appear to be as important or more important than silica dust (Higgins et al. 1959; Gamble et al. 1979; Manfreda et al. 1982; Graham et al. 1984). Two of these studies found lung function to be somewhat better among exposed workers than among reference subjects (Clark et al. 1980; Graham et al. 1984). However, in both of these studies, one of potash miners and one of taconite miners, it is very likely that the free silica exposure, although not documented, was low. One study of fluorspar miners (Parsons et al. 1964) and one of copper miners (Federspiel et al. 1980) suggest a significant dust effect on bronchitis prevalence and a somewhat lower lung function among exposed miners. Specific environmental data on free silica content or dust concentration were not provided in either study, although most likely some of the dust exposure in these mines was silica.

Four of the studies reviewed in Table 3 have documented significant exposures to free silica with the relative absence of other exposures: the Welsh slate workers study (Glover et al. 1980), the Vermont granite workers study (Theriault, Burgess et al. 1974; Theriault, Peters, Fine 1974; Theriault, Peters, Johnson 1974) and two studies of South African gold miners (Sluis-Cremer et al. 1967; Wiles and Faure 1977). Silicosis was reported in all four study populations, ranging from 5 to 33 percent. Sluis-Cremer and colleagues (1967) surveyed the prevalence of chronic bronchitis in a mixed mining and nonmining population in Carletonville on the Witwatersrand, South Africa. Chronic bronchitis was more common among miners who smoked than among nonminers who smoked, but there were no significant differences in prevalence of bronchitis between miners and nonminers who did not smoke. The prevalence of bronchitis was substantially higher among smokers than among

TABLE 3.—Major cross-sectional studies of workers occupationally exposed to silica

Study, country	Number and type of population	Age (mean or range)	Bronchitis (ratio)		Lung function						Pneumoconiosis (percent)	Comment
			S/NS	Exp/Not	S	NS	Δ	Exp	Not	Δ		
Higgins et al. (1959), United Kingdom	Current and ex-foundry workers; 105 exposed, 81 nondusty occupations	55 to 64	Not available for foundry workers alone	1.2	Not available for foundry workers alone			82.1 (Indirect MBC based on $FEV_{75\%}$)	90	-7.9	14.0	Foundry workers both "pure" with free silica exposure and "mixed" with chemical fumes (HCl, H_2SO_4, caustic soda, and benzol) and other dusts; increased respiratory symptoms and decreased lung function mainly in "mixed" foundry workers suggests other dusts and fumes likely more important than "pure" foundry work
Parsons et al. (1964), Canada	Fluorspar mining; 301 exposed, 56 controls	38.8 (20 to 70)	Not available	5.5	Generally higher for nonminers; decreased lung function in chronic bronchitic men appears more important than dust category (based on indirect MBC, MMF, PFR)						1.93	No specific SiO_2 exposures or dust measurements available; exposure determined from job category and tenure
Sluis-Cremer et al. (1967), South Africa	Gold mining; 562 exposed, 265 community controls	35 and older	1.8	1.22	Not studied						5	Free silica content range 50–70%, but generally low dust levels; smoking somewhat more common among miners; significant increase in chronic bronchitis prevalence among smoking and ex-smoking but not nonsmoking miners suggests possible interaction between smoking and "underground aerial pollution"

TABLE 3.—Continued

Study, country	Number and type of population	Age (mean or range)	Bronchitis (ratio)		Lung function						Pneumoconiosis (percent)	Comment
			S/NS	Exp/Not	S	NS	Δ	Exp	Not	Δ		
Higgins et al. (1968), United Kingdom	80 foundry workers, 100 "nondusty" workers	25 to 34	Not reported	Not reported	Not reported separately for foundrymen			3.49	3.55	-.06	23.1	No environmental measurements, but typical SiO_2 foundry exposures; 9-year followup mortality higher among foundry workers than others, appreciably higher among foundry workers with silicosis
	43 foundry workers, 52 "nondusty" workers	55 to 64[1]						2.27 ($FEV_{75\%}$)	2.36	-.09		
Theriault et al. (3 papers) (1974), United States	792 granite workers	44	Not reported	Not reported	4.2 (FVC)	4.1	+.10	4.2	4.1	+.10	31	Single "A" radiograph reader; dose–response relationship between FVC and granite dust and quartz dust; 2 mL FVC/dust-year decline, 9 mL FVC/smoking-year decline
	189 marble workers	47										
Wiles and Faure (1977), South Africa	2,209 gold miners with ≥10 years' service	45 to 54	2.3	5.3 (low dust vs. high dust categories)	2.53	3.77 (MMEF)	-1.24	3.60	3.84 (low dust vs. high dust categories)	-.24	6.7	70–250 particles/cm^3 dust counts; 75% free SiO_2; significant dust exposure/chronic bronchitis dose–response relationship in all smoking categories; much stronger smoking effect on lung function, but no dose–response relationship

TABLE 3.—Continued

Study, country	Number and type of population	Age (mean or range)	Bronchitis (ratio)		Lung function						Pneumoconiosis (percent)	Comment
			S/NS	Exp/Not	S	NS	Δ	Exp	Not	Δ		
Gamble et al. (1979), United States	121 talc miners	39.7	3.5	1.2	3.74	4.13	-.39	3.68	3.84	-.14	2.2 talc, .007 potash	20–40 μg/m³ free silica; 0.23–2.96 mg/m³ respirable dust; anthophyllite, tremolite, and crysotile asbestos fibers found; 17/24 jobs >2f/cc; decreased lung function and pleural thickening significantly associated
	1,077 potash miners (reference group)	39.2				(FEV_1)						
Clark et al. (1980), United States	240 iron ore miners, ≥20 years underground	49.3	None among nonsmoking miners reported	1.0	@78.5	81.4	-2.9	@81.4	80.0	+1.4	<2	Taconite has iron, quartz, and numerous silicates, esp. grunerite-cummingtonite; 25–40% total dust quartz; significant smoking effect, no dust effect on lung function
	86 not exposed	50.1				(FEV_1/FVC)						
Federspiel et al. (1980), United States	133 surface workers	Not given	@8.4	None among nonsmoking nonminers	@85.5	92.5	-7.0	@92.5	98.0	-5.5	Not reported	No dust level or SiO_2% data; no SO_2 miner exposure, little or no surface worker SO_2 exposure; mining and smoking additive effect on bronchitis; significantly reduced nonsmoking miner FEV_1 and FVC and smoking miner FVC
	112 copper miners					(FEV_1)						

TABLE 3.—Continued

Study, country	Number and type of population	Age (mean or range)	Bronchitis (ratio)		Lung function						Pneumoconiosis (percent)	Comment
			S/NS	Exp/Not	S	NS	Δ	Exp	Not	Δ		
Glover et al. (1980), United Kingdom	725 slate workers 530 nonexposed	>18 ≥30	1.8	4.4	3.06 (FEV_1)	3.23	−.17	3.23	3.53	−.30	33	13–32% respirable quartz in respirable dust; no smoking category/radiographic opacity association; no dust concentrations available, but thought "high"; respiratory symptoms dependent on pneumonconiosis category per multiple regression, except nonsmokers with previous TB (in 40–50% of slate workers age >55)
Manfreda et al. (1982), Canada	241 hardrock miners 382 nonexposed men (community sample)	25 to 54	9.0	9.5	23 (Prevalence of FEV_1 abnormalities based on 95th percentile of nonsmoking general population)	7	+16	0	7	−7	<1	Zinc, copper, nickel mining study; 6–9% silica in dust, 20–25% >TLV; some underground worker (95) NO_2 exposure, some smelter worker (107) SO_2 exposure (10% >TLV); low surface worker (39) dust exposure; nonsmoking miner bronchitis significantly increased; significantly reduced lung function in smelter workers, not miners; probable selection processes noted

NOTE: Bronchitis ratios and lung function comparisons are of nonexposed smokers (S) and nonsmokers (NS) to assess smoking effect and of nonsmoking exposed workers (Exp) and nonexposed workers (Not) to assess exposure effect. Combined smoking and exposure effects are not shown, but are addressed under comment.

nonsmokers in both the dust-exposed and the nonexposed populations. Evaluation of Vermont granite shed workers (Theriault, Burgess et al. 1974; Theriault, Peters, Fine 1974; Theriault, Peters, Johnson 1974) revealed that both smoking and cumulative dust exposure contributed to the differences in FVC and FEV_1 among these workers, but the effect of smoking was larger than the effect of dust exposure, using a multiple regression technique. A dose–response relationship between silica dust exposure and decreased lung function was demonstrated in both the Vermont granite shed workers and the South African gold miners (Wiles and Faure 1977). Glover and colleagues (1980) examined 725 workers and former workers from the slate mines and quarries of North Wales and 530 men from the same area who had never been exposed. The prevalence of chronic cough ranged from 5.2 percent in the nonsmokers not exposed to dust to 19.4 percent in the nonsmokers with dust exposure. Smokers with no exposure to dust had a prevalence of cough of 27.5 percent; the prevalence was 38.9 percent among the smokers with dust exposure. FEV_1 (standardized to a fixed height) was lower in the smokers than in the nonsmokers. The dust-exposed nonsmoking workers had a lower mean FEV_1, but the values for the dust-exposed and the nonexposed smokers were similar. The regression coefficients for FEV_1 with age were 20 mL per year in the nonexposed nonsmokers and 38 mL per year in the dust-exposed nonsmokers, but the coefficients for smokers were similar between the dust-exposed (40 mL/year) and nonexposed (46 mL/year) men. The absence of an effect of dust exposure among the smokers in some of these studies may be the result of the cessation of smoking by those workers with declining lung function, as suggested by the observation that the mean FEV_1 and regression coefficient for decline in FEV_1 with age among slate workers was worse in ex-smokers than in either current smokers or nonsmokers. In contrast, the values for ex-smokers in the general population were between those for smokers and those for nonsmokers.

Only a few prospective studies of silica-exposed workers have been reported in the literature. Four of these studies are summarized in Table 4 (Higgins et al. 1968; Pham et al. 1979; Kauffmann et al. 1982; Manfreda et al. 1984). Two other prospective studies of silica-exposed workers are not included in this table because of methodological questions. Brinkman and colleagues (1972) followed a group of foundry workers with silica exposure and with silicosis over an 11-year period. Only a third of the men known not to have died in that interval were restudied, however, raising questions about the validity of the finding of no apparent difference between the silica-exposed workers and the unexposed workers in decline in lung function over time. The original cross-sectional study found poorer lung function among silica-exposed workers and silicotics. Musk and

colleagues (1977) conducted a 4-year followup study of Vermont granite workers and reported a substantially higher annual loss in lung function than predicted from previous cross-sectional studies of this population. However, reassessment of some of these data has raised questions about the adequacy of the pulmonary function testing (Graham et al. 1981). Reanalysis of the population revealed that Vermont granite workers had an annual decline in FEV_1 of 44 mL per year and those who had left the industry had a decline of 72 mL per year (Eisen et al. 1983). The smoking habits of those who continued working (20 pack-years) and those who had left the industry (27 pack-years) were similar. There was no statistically significant relationship between lifetime dust exposure and decline in FEV_1 for either the workers who were still working or those who had left the industry.

One of the four studies reviewed in Table 4 found no increased decline in lung function over time among silica-exposed workers (Higgins et al. 1968). On followup, however, the mortality rate among the foundrymen in the original study (Table 3) was appreciably higher, particularly among those with silicosis and among older workers. Smoking habits were recorded in this study, and the foundry workers who smoked had lower mean FEV_1 values than the nonsmoking foundry workers in both the 25 to 34 and the 55 to 64 age groups. Pham and colleagues (1979) found consistently increased declines with age in all measures of lung function studied (FEV_1, FVC/FEV_1, RV/TLC, and fractional uptake of CO) among silica-exposed steel workers compared with unexposed workers. Results for smoking and nonsmoking workers were not reported separately. Lung function of the exposed men in the original survey was somewhat higher than in the unexposed workers (although they had much more bronchitis), suggesting that selection processes (healthy worker effect) occurred in this study. Kauffmann and colleagues (1979, 1982) also found increased declines in smoking-adjusted lung function over time among workers exposed to mineral dust (especially silica), and argued that the mineral dust and silica exposures were most likely to be causal. Their findings are consistent with this conclusion, but exposures were assessed by type of job, and information on silica dose or interval progression over the 12 years of study is lacking. Manfreda and colleagues (1984), in a 5-year followup study of hard-rock miners and smelter workers, reported significant declines in FEV_1/FVC for both smoking and mining industry exposure. These effects were quantitatively similar, but may reflect more of a smelter effect than a mining (silica dust) effect, as that was the finding on their original cross-sectional study. The prospective study abstract does not address this question.

TABLE 4.—Prospective studies of workers occupationally exposed to silica

Study, country	Number and type of population	Age (mean or range)	Annual decline in lung function						Comments
			S	NS	Δ	Exp	Not	Δ	
Higgins et al. (1968), United Kingdom	80 foundry workers, 100 "nondusty" workers	25–34	38*	21	−17	29	30	−1	Somewhat higher increased annual lung function decline in older men, not strongly associated with occupation, but strongly influenced by smoking
	43 foundry workers, 100 "nondusty" workers	55–74 (Ages in 1957)	32*	54 ($FEV_{.75}$)	−22	37	34	+3	*Heavy smokers only
Pham et al. (1979), France	196 steel (foundry and roll sheet) workers	49.5				7.4%	0.6%	−6.8%	At baseline, bronchitis prevalence significantly higher in steel vs. unexposed workers (37.8 vs. 17.5), lung function somewhat higher in steel workers; over 5-year followup, somewhat more increased steel worker bronchitis prevalence (45.3/21.9); more steelworker than unexposed worker all-parameter lung function consistent decline; no silica content or dust concentration environmental data
	186 unexposed workers	49.8 (Ages at first exam)				(%FEV predicted) Matched for age, height, smoking status			

TABLE 4.—Continued

Study, country	Number and type of population	Age (mean or range)	Annual decline in lung function						Comments
			S	NS	Δ	Exp	Not	Δ	
Kauffmann et al. (1982), France	178 mineral dust exposed workers (55 exposed to silica)	41 (41)*	No smoking-specific lung function decline given			52 (57)	42 (42)	-10 (-15)	12-year followup study of 11 factories, including several mineral dust exposures, of which only silica is separable; no silica monitoring data; significant FEV_1 annual adjusted declines in mineral dust exposed workers (esp. silica exposed) interpreted as work related and consistent with silica-exposed worker original cross-sectional decreased lung function assessment
	177 unexposed workers	41				(FEV_1) Annual declines adjusted for smoking status and amount			* Numbers in parentheses, of 55 silica-exposed workers only
Manfreda et al. (1984), Canada	179 hard rock miners, 254 unexposed (community sample)	25–54	3.4% (Percentage decrease in FEV_1/FVC, over 5 years, adjusted for age and height)	2.0%	-1.4%	3.1% (Percentage decrease in FEV_1/FVC, over 5 years, adjusted for age, height, and smoking)	1.6%	-1.5%	(See Table 2 for cross-sectional results) Cough and phlegm prevalence greater among miners at baseline, no change over time; adjusted FEV_1 and FEV_1/FVC declines significant for smoking and FEV_1/FVC decline significant for mining exposure; data suggest FEV_1/FVC more sensitive indicator; data consistent with mining and smelter exposure and smoking additive effect

NOTE: S = Smoker; NS = Nonsmoker; Exp = Exposed; Not = Not exposed.

Pathogenesis of Silica-Related Health Effects

The characteristic pathology of the various forms of silicosis are well described in recent texts dealing with occupational respiratory diseases (Parkes 1982; Kleinerman and Merchant 1983). The mature lesion of silicosis is the hyalinized nodule that is spherical and typically varies in size from 3 to 12 mm. The nodules are more commonly found in upper lobes, but are found throughout the lung and are frequently subpleural. Microscopically, the nodules have a whorled appearance composed of lamina of acellular hyalin. The borders of the lesions are typically serpiginous and are composed of pigment (especially if associated with a coal exposure), chronic inflammatory cells (mainly lymphocytes and plasmacytes), and connective tissue extending into the surrounding lung parenchyma. With phase microscopy, doubly refractile silica particles 1 to 5 μm in size may be observed within the lesions and within macrophages in the surrounding infiltrate.

Acute silicosis, or acute silicoproteinosis, differs from classical nodular silicosis in that the principal finding is alveolar proteinosis associated with a diffuse interstitial reaction. Scanning electron microscopy and x-ray microanalysis have demonstrated small birefringent silica and silicate particles (less than 1 μm in diameter) in these processes (Abraham 1978, 1984).

Progressive massive fibrosis may develop on a background of silicosis through the enlargement and sometimes the coalescence of the nodular lesions of silicosis into conglomerate silicosis. These lesions form most commonly in the apical or middle portion of the upper lobes and are frequently complicated by tuberculosis. Cavitation of these lesions may occur with or without tuberculous infection (Kleinerman and Merchant 1983).

The mechanisms that produce silicosis, and particularly conglomerate silicosis, are still not fully understood. The cellular events leading to lung injury appear to arise from the cytotoxicity of the respirable silica particle for a principal lung defender, the alveolar macrophage. Upon phagocytosis of the silica particle, cell death is caused by the release of proteolytic and hydrolytic enzymes into macrophage cytoplasm. The release of these cytoplasmic constituents, including the still biologically active silica particle and fibroblast stimulating factor, may then lead to fibrosis (Allison et al. 1966, 1977).

As has been noted with other types of pneumoconiosis, silicosis (and particularly conglomerate silicosis) is associated with a high prevalence of circulating autoantibodies (ANA and RF) (Jones et al. 1976; Turner-Warwick et al. 1977). Although silica exposure and particularly silicosis may be associated with rheumatoid arthritis and several other collagen-vascular diseases, the role of these antibodies in the etiology, onset, and progression of silicosis is not

clear (Parkes 1982). Angiotensin$_1$-converting enzyme (ACE) elevation has also been reported among silicotics (Gronhagen-Riska 1979; Nordman et al. 1984). Nordman and colleagues (1984), in a case–reference study of the Finnish Occupational Diseases Register from 1965 to 1977, reported an association between ACE activity and progression of silicosis. Smoking, age, and bronchitis were not related to ACE activity, which was thought to reflect accumulation and increased degradation of macrophages. Histocompatibility antigens (HLA) have also been studied as possible genetic risk factors for silicosis, but with variable results. Koskinen and colleagues (1983) found that the prevalence of HLA-AW19 was higher in their Finnish silicosis patients than in the silica-exposed referent population and that the highest risk of developing advanced silicosis was associated with the phenotypic combination AW19 and B18. However, Sluis-Cremer and Maier (1984) reported only a decrease in HLA-B40 among 45 South African gold miners. These variable associations are statistically weak and may be related to the number of statistical tests performed on the multiple HLA antigens.

The pathogenesis of airways obstruction in silica-exposed workers is less well understood. Although increased rates of bronchitis and decreased lung function have been observed in epidemiological studies comparing silica-exposed and unexposed workers, it appears that these findings are largely separate from the clinical and epidemiological picture of silicosis. In the largest and best controlled study of a reasonably pure silica-exposed sample of 1,973 white gold miners (Irwig and Rocks 1978), chronic bronchitis was found to be equally common among those with radiographic evidence of silicosis and those without. The smoking habits of miners with radiographic silicosis and of those without silicosis were not significantly different statistically. Silicotics reported only more days away from work, a finding the authors suggested may have been as related to their compensation status as to their disease. Comparison of lung function between silicotics and their silica-exposed referants revealed equivalent FVC, FEV_1, and $FEF_{25-75\%}$ among silicotics.

Recent pathological evidence of a nonfibrous mineral dust small airway lesion has been provided by Churg and Wright (1983). This pathological process, which they labeled mineral dust airways disease (MDAD), is similar to that produced by tobacco smoke. This pathological process involves primarily respiratory bronchioles, with a lesser extension into alveolar ducts. This lesion generally involves more pigmentation and more thickening of the bronchiole walls than is typically found in cigarette smokers. In a recent study by Churg and colleagues (1985) of 13 cases of patients with MDAD, 7 had occupational histories consistent with a primary silica exposure. Only 1 of 121 cases without a clear history of dust exposure was found to have MDAD. Those with MDAD, matched for age and

smoking habit with 13 cases without MDAD, were found to have significantly poorer lung function, including clinically relevant lower mean levels of FEV_1, $FEF_{25-75\%}$, and FVC and increased RV/TLC and ΔN_2 per liter as percentages of that predicted. It was also noted that significantly more membranous and respiratory bronchiole fibrosis occurred among subjects with MDAD. The similarity in location, morphology, and physiological impairment between the pathology induced by mineral dust and that observed with cigarette smoking suggests that the cellular events giving rise to them may be similar. Although a good deal is known about the pathogenesis of the process arising from cigarette smoke (US DHHS 1984), systematic experimental studies of mineral dust airways disease have not been reported.

Silica Exposure and Cancer

Initial concerns about the association between silica exposure and cancer arose during the 1930s among investigators in England, Canada, and South Africa. In the early research on this topic, the focus was on the proportion of lung cancers arising among autopsied cases of silicosis compared with that among nonsilicotics or members of the general public. All of the early research (Dible 1934: Anderson and Dible 1938; Kennaway and Kennaway 1947; Klotz 1939; Irvine 1939) was characterized by the lack of any data on smoking.

Early assessments of the association between silicosis and lung cancer were summarized by Hueper (1966). More recently, Heppleston (1985) summarized the autopsy findings from South Africa (Becker and Chatgidakis 1960; Chatgidakis 1963), from Switzerland (Ruttner and Heer 1969), and from Germany (Otto and Hinuber 1972), but again no smoking data were presented. The reports from South Africa and Switzerland showed no differences in the ratio of lung cancers between silicotics and controls. However, Otto and Hinuber (1972) showed that porcelain workers with silicosis had more than twice the proportion of lung cancers as the noncases. Early studies suggested that silicotics have an increased lung cancer risk (Dible 1934; Klotz 1939; Mittmann 1959) or that silicotics with respiratory cancer have greater concentrations of silica in lung tissue (Anderson and Dible 1938). However, data from Bridge (1938), Heppleston (1985), Hueper (1966), and Irvine (1939) suggested that lung cancer risk among silicotics is less than or equal to that of men without silicosis, regardless of their occupation. In reviewing the evidence, Hueper (1966) observed that the data support the idea that lung cancer is a coincidental finding among silicotics and that there is no etiological relationship.

None of these studies addressed the smoking status of the subjects, a crucial omission in any study of lung cancer. Furthermore, age was

not adjusted, nor were there any quantitative estimates of the silica exposure or assessments of the severity of the silicotic lesions.

Epidemiologic Studies of Smoking, Silica Exposure, Silicosis, and Cancer

Silica-Exposed Cohort Studies

Occupational silica dust exposure is common in many industries; therefore this section is organized so that exposure studies in work settings that are similar can be examined together, i.e., metal ore mining, the steel industry, and workplaces where exposures are to silica only.

Metal Ore Mining

McDonald and colleagues (1978) conducted an enlarged followup study from 1937 to 1973 of the Homestake Veterans Association cohort that included 1,321 men with at least 21 years of employment at the mine. Standardized mortality ratios (SMRs) were calculated using South Dakota mortality rates as opposed to U.S. rates. The South Dakota lung cancer rates were lower than those for the United States as a whole. Using dust exposure data from company midget impinger samples, the authors examined the pneumoconiosis (mostly silicosis) and cancer risks in five categories of dustiness, collapsing them when indicated owing to small numbers. The data showed striking trends for pneumoconiosis and tuberculosis, but no gradients emerged for respiratory cancer.

Brown and colleagues (1985) also conducted an assessment of the Homestake gold miners. The cohort included 3,328 white male miners employed at least 1 year between 1940 and 1965 and followed until June 1, 1977. The authors calculated SMRs using person-years and contrasted mine mortality rates with rates for U.S. white men. An index of dust exposure by job location was assembled for the purpose of assessing dose–response gradients. The SMR for malignant neoplasms of the trachea, bronchus, and lung was 100, with no trends in latency or dust exposure by length of employment.

Katsnelson and Mokronosova (1979) examined the mortality at a U.S.S.R. gold mine and at several brick plants from 1948 to 1974. Dust concentrations were not specifically stated for workers in the gold mine, and an approximation of the SMR (which the authors termed "relative risk") was calculated to compare the cancer risk among gold miners with the cancer risk of residents of a nearby town (excluding those who worked with chromate dusts and adding to the comparison group those who worked less than 3 years in the plants under study). The authors reported a relative risk (RR) of 7.9 ($p < 0.001$) for lung cancer among the male underground gold miners; without the silicotics, the RR was 3.1 ($p < 0.02$). Surface workers had

a nonsignificant RR of 1.6. No lung cancer deaths occurred among women during these years. No smoking data were presented for gold mine workers, although data presented for workers at a silica firebrick plant and an aluminosilicate brick plant indicated that two-thirds to three-fourths of the men smoked, whereas only 0 to 15 percent of the women did. There appeared to be an inverse gradient of the proportion of lung cancers by stage of silicosis or silicotuberculosis (although no standard classification such as that of International Labour Office (1980) is given).

Armstrong and colleagues (1979) followed 1,974 Kalgoorlie gold miners from Western Australia (whose smoking habits were measured between 1960 and 1962) for silicosis incidence and mortality through 1975. Expected death rates were obtained from the age-specific death rates of Western Australia during 1963–1967, 1968–1972, and 1972–1976. There were significant ($p < 0.01$) mortality excesses for respiratory cancer (SMR 140) and for pneumoconoisis and silicosis (SMR 640). The authors compared the cancer risk of the underground miners and the surface miners and also the association between silicosis, smoking, and lung cancer. They observed a 40 percent excess of lung cancer among underground workers and a 13 percent excess risk of pulmonary cancer among silicotics (both nonsignificant). In 1961–1962, the Kalgoorlie miners had a greater prevalence of smoking (66.3 percent) than either the coal miners (58.7 percent) or the male residents of Busselton, Australia, in 1966 (53.2 percent) and tended to smoke more cigarettes per day. The authors stated that the lung cancer risk was probably a function of the heavier cigarette smoking habits of the miners and that there was little evidence to link experience underground (and thus exposure to silica) to lung cancer risk.

Costello (1982) conducted a followup study of 12,258 white "metal ore" miners who were part of a 1958–1961 U.S. Public Health Service (US PHS) survey of silicosis and the metal mining industry. SMRs were calculated using as expected values the 1968 through 1970 white male mortality rates in the 16 States where the mines were located. The results showed that the cohort as a whole had an all-causes SMR of 105.9 ($p < 0.01$); the SMR for cancer of the trachea, bronchus, and lung was 126.6 ($p < 0.001$), and the SMR for pneumoconiosis (mostly silicosis) was 343.6 ($p < 0.001$). Both digestive tract cancers and hypertensive heart disease were significantly reduced. Costello presented several cause-specific and ore-specific SMRs that were all significant at $p < 0.05$. Respiratory cancer SMRs were 130.0 among lead zinc miners, 354.6 for mercury miners, and 346.5 for chromium miners. Highly statistically significant SMRs for pneumoconiosis were obtained among copper, lead zinc, molybdenum, and gold or silver ore miners. In the US PHS 1958–1961 survey, 14.5 percent of the metal miners were nonsmokers, 10.9 percent were ex-

smokers, 70.5 percent were current smokers, and 37 percent were pipe and cigar smokers. The smoking status of 0.4 percent was unknown. Costello argued that on the basis of a relationship between lung function tests and lung cancer, cigarette smoking was the major predictor of excess lung cancer in these metal ore miners.

Steel Industry

Gibson and colleagues (1977) conducted a retrospective cohort study of the Dofasco steel mill workers in Hamilton, Ontario, Canada, from 1967 to 1976. The authors compared foundry workers with nonfoundry workers and reported a lung cancer SMR of 250 ($p < 0.0005$). They used metropolitan Toronto male mortality rates to calculate expected values. The authors noted that the finishing area had the highest mean level of total suspended particulates (much of it silica), respirable particulates, and benzene-soluble fraction of total suspended particulates. The molding and furnace work areas had similar industrial hygiene characteristics. No smoking histories were available for the cohort as a whole. However, 22 of the 24 men with lung cancers were cigarette smokers. The authors proposed that smoking and particulate exposure (containing adsorbed organic material) might be an explanation for the excess lung cancers.

Blot and colleagues (1983) conducted a case–control study of lung cancer among white men in eastern Pennsylvania to assess the association with employment in the steel industry. Interviews with next of kin provided information about residential, occupational, and smoking histories. The authors demonstrated a smoking-adjusted odds ratio of 2.2 for usual employment in the steel industry (95 percent confidence interval, 1.5 to 3.3). The odds ratio for lung cancer was also calculated by smoking category and was significantly elevated for light smokers and heavy smokers but not for nonsmokers or for moderate smokers.

Workplaces With Exposure to Silica Only

In contrast with workers in the foundry and mining industries, where silica exposure is most likely to be "contaminated" by combination with organic foundry fumes or asbestiform materials, or radon in the case of mining, some workers are exposed to "pure" silica. These workers are found in several industries, including ceramics or firebrick manufacture, granite quarrying, or tunnel digging.

Katsnelson and Mokronosova (1979) examined lung cancer at two aluminosilicate fireclay plants and at a silica firebrick plant. Although the firebricks and the fireclay dusts contain high levels of quartz, no dust samples were collected in the plants. The relative risk (RR) for lung cancer for the male workers was 4.0 ($p < 0.01$) and

4.5, respectively, at the fireclay plants, and a nonsignificant SMR of 5.1 was reported for the female workers at the first plant. At the firebrick plants the RR was 2.0 ($p < 0.05$) for male workers and 0.8 for the female workers.

Vermont granite workers are exposed to quartz dust with a concentration of approximately 30 percent free silica. Davis and colleagues (1983) conducted a proportional morbidity rate (PMR) study of 969 deceased white granite workers whose x rays were on file at the Vermont Division of Industrial Hygiene and who had died between 1952 and 1978. The authors developed a dust exposure index for the purpose of assessing exposure profiles for their study subjects. They analyzed the data, excluding tuberculosis and silicosis after both of these causes of death showed powerful excess disease risks. Slight excesses for digestive tract, lung, larynx, and prostate cancers were reported, including a PMR of 1.3 for general respiratory cancer (95 percent confidence intervals, 1.0 to 1.6). No apparent trends emerged relating dust exposure categories with either digestive cancer, respiratory diseases, or lung cancer. Smoking data were not available for the subjects.

Costello and Graham (1985) conducted a cohort study of 5,414 Vermont granite workers from 1950 to 1982. The authors used the personnel information on file in the Occupational Hygiene Division of the Vermont State Health Department to ascertain date of hire and date of death. Significant overall excess mortality was observed for silicosis (SMR 586.6) and tuberculosis (SMR 473.8), but the excesses were confined to workers hired before 1940. However, no increased risks were observed for either respiratory system cancer or lung cancer. The latency time may have been too short to determine the lung cancer risk among granite workers hired after 1940. Information was lacking on smoking and dust exposure, and the Vermont records regarding employees at risk were incomplete.

Selikoff (1978) examined a 932-man cohort of unionized New York City tunnel workers from 1955 to 1972. These men were exposed to silicious dusts containing sizable amounts of quartz, schists, and gneises, but there was little likelihood of exposure to asbestos. There was an SMR of 495 for pulmonary tuberculosis, an SMR of 160 for lung cancer, and a gradient in the risk of respiratory cancer according to the number of years worked. No smoking data were available, and it is possible that this elevated risk may be a reflection only of long-term smoking habits and not of silica exposure.

Followup of Silicotics

Westerholm (1980) conducted a followup study from 1931 to 1969 of silicotics from the Swedish Pneumoconiosis Register. For those whose silicosis arose from employment in mining, quarrying, or tunneling (MQT) and whose silicosis was diagnosed between 1931

and 1948, the lung cancer PMR was 590 ($p<0.01$); for MQT workers whose silicosis was diagnosed between 1949 and 1969, the PMR was 380 ($p<0.01$). The other significant finding was among workers in the steel and iron industry (SII) whose silicosis occurred between 1949 and 1969; their PMR was 220 ($p<0.05$). Westerholm and colleagues (1985) extended the study from 1961 to 1980 to follow up 712 silicosis cases and 810 noncases from the Swedish silica exposure registry, matched for age, industry, and occupation. For MQT workers, the SMR was 538 ($p<0.05$) and for SII workers, 385 ($p<0.05$). Smoking was not adjusted in the first study, and in the second, it was indirectly accounted for by the selection of controls from the same cohort as the silicosis cases.

Finkelstein and colleagues (1982) studied 1,190 Ontario, Canada, silicotic miners diagnosed between 1940 and 1975. The authors reported an overall SMR of 198 ($p<0.01$), with SMRs of 303 ($p<0.01$) and 195 ($p<0.05$) for silicotics diagnosed between 1940 and 1949 and between 1950 and 1959, respectively. No smoking data were collected.

Schuller and Ruttner (1985) examined the mortality from 1960 to 1978 of 2,399 cases of silicosis in Switzerland. To account for the sequelae of silicosis (such as tuberculosis and cor pulmonale), the authors calculated age- and period-specific mortality odds ratios (MOR). The lung cancer MORs by industry were as follows: miners 229 ($p<0.01$); stone workers 118 ($p<0.6$); foundrymen 327 ($p<0.001$); others plus ceramic workers 237 ($p<0.05$); and ceramic workers 205 ($p=0.25$). The overall MOR for all Swiss silicotics was 223 ($p<0.05$). The authors noted that smoking is a major cofactor because smokers have more chest symptoms, thus making silicosis more easily detected, and because a high proportion of workers in silica-exposed jobs are smokers, ranging from 60 percent to 85 percent. Because of the lack of significant lung cancer risk among stone workers with silicosis (having less confounding exposure to polycyclic aromatic hydrocarbons than workers in foundries), the authors argued against silica being a carcinogen, but postulated an interaction of occupation and smoking. The authors cited the need for cohort studies of workers in these industries with silica exposure, including detailed smoking information. An additional question is the relation of lung cancer risk by degree of silicosis.

Neuberger and colleagues (1985) examined the relative risk for lung cancer among Austrian silicotics from 1955 to 1979. The overall risk adjusted for age and sex was 1.4 ($p<0.05$). The lung cancer relative risk increased from 1.31 in the 1955 to 1959 period to 1.42 in the 1975 to 1979 period. No information was provided on smoking, on industry-specific risks, or on possible silica exposure levels.

Kurppa and colleagues (1985) examined the subsequent mortality of 961 cases of silicosis diagnosed in Finland between 1935 and 1977.

Using the Finnish male population as a comparison group, they observed 80 lung cancer deaths instead of the age-adjusted expected number of 25.6, a SMR of 312 (99 percent confidence interval, 230 to 414). The authors also found SMRs of over 700 for pulmonary disease and tuberculosis. When the lung cancer risk was examined by industry, the SMR results were as follows: mining 436 ($p<0.01$); stone industry 271 ($p<0.01$); steel casting 184; iron foundries 225; and other industries 343 ($p<0.01$). The authors demonstrated that the SMRs for each industry showed a 40 percent or more risk increase (despite small numbers) regardless of whether the silicosis was diagnosed between 1935 and 1959 or between 1960 and 1977. The authors did not have smoking data.

Zambon and colleagues (1985) examined a cohort of 1,234 silicotics from the Veneto region of Italy who were diagnosed from 1959 to 1963, and followed them through 1980. Complete occupational and smoking histories were available. Overall, the cohort had striking excesses of infectious disease (tuberculosis) and respiratory disease (silicosis) mortality, with SMRs of 1,960 and 741, respectively. There was a significant ($p<0.05$) lung cancer SMR of 228 and a nonsignificant SMR of 206 for cancer of the larynx (based on only seven cases). There was a gradient of lung cancer risk using years since first silica exposure as a surrogate for dose (risk did not begin to rise until 20 years after the first exposure). The gradient was maintained across mining and tunneling industries; tunneling and quarrying industries had significant overall SMRs of 239 and 569, respectively. The authors reported that only 13.2 percent of the cohort were nonsmokers and only 3 of 49 deaths occurred in this group; thus, they believed that the excess mortality was very likely due to smoking.

Research Recommendations

1. Further prospective dose–response studies on chronic bronchitis and airways obstruction assessing silica concentration, smoking, and airway reactivity should be undertaken.
2. Systematic, well-controlled studies of lung tissue from silica-exposed workers to assess the pathology and associated impairment of small airways disease should be undertaken.
3. Experimental studies of the interaction of cigarette smoke and silica dust on the pathogenesis of small airways disease should be undertaken.
4. The potential for silica to act as a carcinogen alone or in combination with other exposures should be investigated in carefully controlled studies that include a detailed examination of the smoking habits of the participants.
5. Priority should be given to compliance with the current silica permissible exposure limit.

6. Systematic surveillance of silica-exposed populations to document silica dose and silica-associated health effects should be extended by government agencies, unions, and industry.

Summary and Conclusions

1. Silicosis, acute silicosis, mixed-dust silicosis, silicotuberculosis, and diatomaceous earth pneumoconiosis are causally related to silica exposure as a sole or principal etiological agent.
2. Epidemiological evidence, based on both cross-sectional and prospective studies, demonstrates that silica dust is associated with chronic bronchitis and chronic airways obstruction. Silica dust and smoking are major risk factors and appear to be additive in producing chronic bronchitis and chronic airways obstruction. Most studies indicate that the smoking effect is stronger than the silica dust effect.
3. Pathological studies describe mineral dust airways disease, which is morphologically similar to the small airways lesions caused by cigarette smoking.
4. A number of studies have demonstrated an increased risk of lung cancer in workers exposed to silica, but few of these studies have adequately controlled for smoking. Therefore, while the increased standardized mortality ratios for lung cancer in these populations suggest the need for further investigation of a potential carcinogenic effect of silica exposure (particularly in a combined exposure with other possible carcinogens), the evidence does not currently establish whether silica exposure increases the risk of developing lung cancer in man.
5. Smoking control efforts should be an important concomitant of efforts to reduce the burden of silica-related illness in working populations.

References

ABRAHAM, J.L. Recent advances in pneumoconiosis: The pathologist's role in etiologic diagnosis. In: Thurlbeck, W.M., Abell, M.R. (eds.). *The Lung: Structure. Function and Disease.* International Academy of Pathology, Monographs in Pathology, No. 19. Baltimore, Williams and Wilkins Co., 1978, pp. 96–137.

ABRAHAM, J.L. Identification and quantitative analysis of tissue particulate burden. *Annals of the New York Academy of Sciences* 428:60–67, 1984.

ALLISON, A.C., CLARK, I.A., DAVIES, P. Cellular interactions in fibrogenesis. *Annals of the Rheumatic Diseases* 36(Supp.):8–13, 1977.

ALLISON, A.C., HARINGTON, J.S., BIRBECK, M. An examination of the cytotoxic effects of silica on macrophages. *Journal of Experimental Medicine* 124(2):141–154, August 1, 1966.

ANDERSON, C.S., DIBLE, J.H. Silicosis and carcinoma of the lung. *Journal of Hygiene* 38:185–204, 1938.

ARMSTRONG, B.K., McNULTY, J.C., LEVITT, L.J., WILLIAMS, K.A., HOBBS, M.S.T. Mortality in gold and coal miners in Western Australia with special reference to lung cancer. *British Journal of Industrial Medicine* 36(3):199–205, August 1979.

ASHE, H.B. Silicosis and dust control: Vermont's granite industry. *Public Health Reports* 70(10):983–985, October 1955.

ASHE, H.B., BERGSTROM, D.E. Twenty-six years' experience with dust control in the Vermont granite industry. *Industrial Medicine and Surgery* 34(12):973–978, 1965.

ASPEN SYSTEMS CORPORATION. A guide to toxic exposures by occupation. In: McRae, A., Whelchel, L., Rowland, H. (eds.). *Toxic Substances Control Sourcebook.* National Institute for Occupational Safety and Health, Center for Compliance Information, 1978, pp. 345–366.

AYER, H.E., DEMENT, J.M., BUSCH, K.A., ASHE, H.B., LEVADIE, B.T.H., BURGESS, W.A., DiBERARDINIS, L. A monumental study: Reconstruction of a 1920 granite shed. *American Industrial Hygiene Association Journal* 34(5):206–211, May 1973.

BANKS, D.E., MORRING, K.L., BOEHLECKE, B.A. Silicosis in the 1980's. *American Industrial Hygiene Association Journal* 42(1):77–79, January 1981.

BANKS, D.E., MORRING, K.L., BOEHLECKE, B.A., ALTHOUSE, R.B., MERCHANT, J.A. Silicosis in silica flour workers. *American Review of Respiratory Disease* 124(4):445–450, October 1981.

BECKER, B.J.P., CHATGIDAKIS, C.B. The heart in silicosis. In: Orenstein, A.J. (ed.). *Proceedings of the Pneumoconiosis Conference, Johannesburg, 1959.* Boston, Little, Brown and Co., 1960, pp. 205–216.

BLOT, W.J., BROWN, L.M., POTTERN, L.M., STONE, B.J., FRAUMENI, J.F., Jr. Lung cancer among long-term steel workers. *American Journal of Epidemiology* 117(6):706–716, June 1983.

BRIDGE, J.C., 1938. (Cited in Kennaway and Kennaway 1947).

BRINKMAN, G.L., BLOCK, D.L., CRESS, C. Effects of bronchitis and occupation on pulmonary ventilation over an 11-year period. *Journal of Occupational Medicine* 14(8):615–620, August 1972.

BROWN, D.P., KAPLAN, S.D., ZUMWALDE, R.D., KAPLOWITZ, M., ARCHER, V.E. Retrospective cohort mortality study of underground gold mine workers. In: Goldsmith, D.F., Winn, D.M., Shy, C.M. (eds.). *Silica, Silicosis, and Cancer.* New York, Praeger, 1985, pp. 335–350.

CHATGIDAKIS, C.B. Silicosis in South African white gold miners. *South African Journal of Advanced Medicine and Science* 9:383–392, 1963.

CHURG, A., WRIGHT, J.L. Small-airway lesions in patients exposed to nonasbestos mineral dusts. *Human Pathology* 14(8):688–693, August 1983.

CHURG, A., WRIGHT, J.L., WIGGS, B., PARE, P.D., LAZAR, N. Small airways disease and mineral dust exposure: Prevalence, structure, and function. *American Review of Respiratory Disease* 131(1):139–143, January 1985.

CLARK, T.C., HARRINGTON, V.A., ASTA, J., MORGAN, W.K.C., SARGENT, E.N. Respiratory effects of exposure to dust in taconite mining and processing. *American Review of Respiratory Disease* 121(6):959–966, June 1980.

COSTELLO, J. *Mortality of Metal Miners: A Retrospective Cohort and Case-Control Study.* Paper presented at the Park City, Utah, Environmental Health Conference, April 6–9, 1982.

COSTELLO, J., GRAHAM, W.G.B. Vermont granite workers' mortality study. In: Goldsmith, D.F., Winn, D.M., Shy, C.M., (eds.). *Silica, Silicosis, and Cancer.* New York, Praeger, 1985, pp. 437–440.

DAVIS, L.K., WEGMAN, D.H., MONSON, R.R., FROINES, J. Mortality experience of Vermont granite workers. *American Journal of Industrial Medicine* 4(6):705–723, 1983.

DIBLE, J.H. Silicosis and malignant disease. *Lancet* 227(2):982–983, 1934.

DREESSEN, W.C., PAGE, R.T., HOUGH, J.W., TRASKO, V.M., JONES, J.L., FRANKS, R.W. *Health and Working Environment of Nonferrous Metal Mine Workers.* Public Health Bulletin No. 277. U.S. Department of Health, Education, and Welfare, Public Health Service, and the Federal Security Agency, 1942.

EISEN, E.A., WEGMAN, D.H., LOUIS, T.A. Effects of selection in a prospective study of forced expiratory volume in Vermont granite workers. *American Review of Respiratory Disease* 128(4):587–591, 1983.

FEDERSPIEL, C.F., LAYNE, J.T., AUER, C., BRUCE, J. Lung function among employees of a copper mine smelter: Lack of effect of chronic sulfur dioxide exposure. *Journal of Occupational Medicine* 22(7):438–444, July 1980.

FINKELSTEIN, M., KUSIAK, R., SURANYI, G. Mortality among miners receiving workmen's compensation for silicosis in Ontario: 1940–1975. *Journal of Occupational Medicine* 24(9):663–667, September 1982.

FLINN, R.H., BRINTON, H.P., DOYLE, H.N., CRALLEY, L.J., HARRIS, R.L., Jr., WESTFIELD, J., BIRD, J.H., BERGER, L.B. *Silicosis in the Metal Mining Industry: A Revaluation, 1958–1961.* U.S. Department of Health, Education, and Welfare, Public Health Service, and U.S. Department of the Interior, Bureau of Mines, PHS Pub. No. 1076, 1963, 238 pp.

FLINN, R.H., DREESSEN, W.C., EDWARDS, T.I., RILEY, E.C., BLOOMFIELD, J.J., SAYERS, R.R., CADDEN, J.F., ROTHMAN, S.C. *Silicosis and Lead Poisoning Among Pottery Workers.* Public Health Bulletin No. 244. U.S. Department of Health, Education, and Welfare, Public Health Service, and the Federal Security Agency, 1939.

FOX, A.J., GOLDBLATT, P., KINLEN, L.J. A study of the mortality of Cornish tin miners. *British Journal of Industrial Medicine* 38(4):378-380, November 1981.

FULTON, W.B., BUTTERS, F.E., DOOLEY, H.E., KOPPENHAVEN, F.B., MATHEWS, J.L., KIRK, R.M. *A Study of Silicosis in the Silica Brick Industry.* Harrisburg, Commonwealth of Pennsylvania, Department of Health, Bureau of Industrial Hygiene, 1941, 60 pp.

GAMBLE, J.F., FELLNER, W., DIMEO, M.J. An epidemiologic study of a group of talc workers. *American Review of Respiratory Disease* 119(5):741–753, May 1979.

GIBSON, E.S., MARTIN, R.H., LOCKINGTON, J.N. Lung cancer mortality in a steel foundry. *Journal of Occupational Medicine* 19(12):807–812, December 1977.

GLOVER, J.R., BEVAN, C., COTES, J.E., ELWOOD, P.C., HODGES, N.G., KELL, R.L., LOWE, C.R., McDERMOTT, M., OLDHAM, P.D. Effects of exposure to slate dust in North Wales. *British Journal of Industrial Medicine* 37(2):152–162, May 1980.